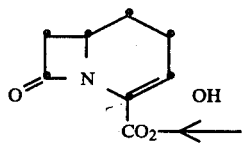
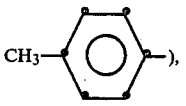
Tert-Butyl
6(R)-3-p-toluenesulfonyloxy-8-Oxo-1-Azabicyclo[4,2,-0]oct-2-ene-2-carboxylate

A mixture of 4(R)-4-[4-(t-butyloxycarbonyl)-4-diazo-3-oxobutyl]azetidin-2-one (1.75 g, 6.55 mmol) and rhodium (II) acetate (17 mg) in 130 ml of degassed benzene is heated at 75°–80° C. until t.l.c. analysis (ethyl acetate) shows no remaining starting material. The mixture is cooled to room temperature, filtered, and concentrated in vacuo to yield tert-butyl 6(R), 3-hydroxy-8-oxo-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate.



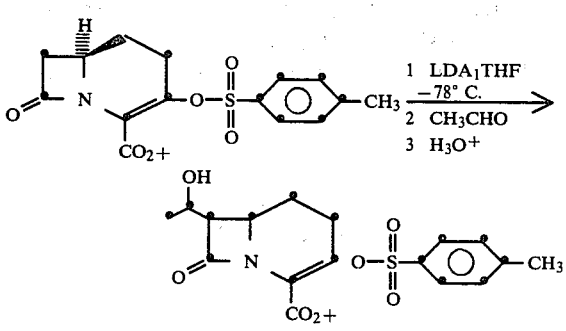
This material is redissolved in 35 ml of dry methylene chloride and cooled to 0° C. prior to the successive addition of p-toluenesulfonic anhydride (2.56 g, 7.86 mmol) and triethylamine (795 mg. 7.86 mmol). The resulting solution is stirred at 0° C. for 45 min., then diluted with ethyl acetate and washed with 2% aqueous hydrochloric acid solution, water and brine and dried over anhydrous magnesium sulfate. The solvent is removed in vacuo to give a viscous oil which is chromatographed on 100 g of silica gel (ether) to yield a white solid. This material is recrystallized from ether-petroleum ether to yield 1.79 g (70%) of tert butyl 6(R)-3-p-toluenesulfonyloxy-8-oxo-1-azabicyclo[4,2,0]oct-2-ene-2-carboxylate as white flakes: m.p. 99°–100° C.; $[\alpha]_D = +132.5°$ (C=3.57, $CHCl_3$); I.R. ($CHCl_3$) 1772, 1725, 1600, 1155, H NMR ($CDCl_3$) δ 7.61 (AA' BB', 4H, aromatic), δ 3.64 (m, 1H, H6), δ 3.28 (dd, J=15.2, 5, 1H, H7b), δ 2.64 (dd, J=15.2 2.3, 1H, H7a), δ 2.4–2.55 (m, 1H, H4a or b), δ 2.45 (s, 3H,



δ 2.23 (m, 1H, H4a or b), δ 1.3–1.7 (m, 2H, H5a & b), δ 1.49 (s, 9H,tBu); mass spectrum m/e 393(M+), 337, 320, 292, 238, 182, 155.

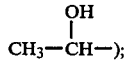
Anal calcd for $C_{19}H_{23}NO_6S$: C, 58.00; H, 5.89; N, 3.56; S, 8.15. Found: C, 57.98; H, 5.99; N, 3.34; S, 7.80.

STEP H

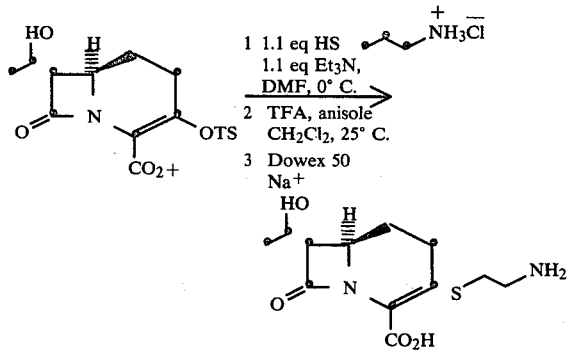


Tert Butyl 6(R),
7(S)-3-p-toluenesulfonyloxy-7-[1-(R)hydroxyethyl]-8-oxo-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate (trans-R isomer)

Butyl lithium (960 μl of a 2.3 M solution, 2.2 mmol) is added by syringe to a solution of diisopropyl amine (223 mg, 2.2 mmol) in 20 ml of freshly distilled tetrahydrofuran at −78° C. The resulting solution is stirred at −78° C. for 15 min. prior to the dropwise addition of a solution of tert-butyl 6(R)-3-p-toluenesulfonyloxy-8-oxo-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate (786 mg, 2.0 mmol) in 2 ml of tetrahydrofuran. The resulting dark orange enolate solution is stirred at −78° C. for 15 min. prior to the addition of acetaldehyde (880 mg, 20 mmol). After an additional 10 min. at −78° C., saturated aqueous ammonium chloride solution is added and the mixture is allowed to warm to room temperature. The reaction mixture is diluted with ethyl acetate (100 ml) and washed with 2% aqueous hydrochloric acid solution, water and brine and dried over anhydrous magnesium sulfate. Removal of the solvents in vacuo gives an oil which is chromatographed on 20 g of silica gel (ethyl ether) to remove polar and non-polar by-products. The product mixture is isolated as a white foam (537 mg). Starting material (37 mg, 5%) is also isolated as a white solid. The product mixture is chromatographed on three 2000μ silica gel GF plates (ether, 4 elutions). The most polar compound is S-trans (277 mg); the intermediate is R-trans (173 mg) and the least polar is a mixture of R and S-cis (80 mg). The total yield based on recovered starting material is 63%. Yield of the desired trans-R is 21%. IR ($CHCl_3$) 1763, 1724 cm^{-1}; NMR ($CDCl_3$) δ 7.62 (AA' BB', 4H, aromatic), δ 4.20 (m, 1H, H8), δ 3.62 (ddd, J=11, 2.1, 2, 1H, H-6), δ 2.87 (dd, J=6.5, 2.1, 1H, H-7), δ 2.46 (s, 3H, CH_3-Ar), δ 2.2–2.4 (m, 2H, H4a & b), δ 1.3–1.7 (m, 2H, H5a & b), δ 1.48 (S, 9H, tBu), δ 1.33 (d, J=6.5,



mass spectrum (m/e) 437 (M+), 381, 364, 336, 282, 226, 182.



Homothienamycin

Triethylamine (23.3 mg, 0.23 mmol) is added by syringe to a mixture of tert-butyl 6(R), 7(S)-3-p-toluenesulfonyloxy-1-[1-(R)-hydroxyethyl]-8-oxo-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate (91 mg, 0.208 mmol) and cysteamine hydrochloride (26 mg, 0.23